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Activation of AMPK by Metformin Inhibits PDGF-induced Proliferation of Renal Fibroblasts

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Background: Platelet-derived growth factor (PDGF) plays an important role in renal interstitial fibrosis (RIF) in chronic kidney disease (CKD). Activation of AMPK has been shown to inhibit the occurrence of renal remodeling in CKD, and yet it remains unknown whether the effect of AMPK on suppression of renal interstitial fibrosis is associated with the inhibition of PDGF signaling.

Methods: In the present study, primary cultured mouse renal fibroblasts were stimulated with PDGF, the selective inhibitor of PI3K or mTOR was applied to investigate the involvement of these pathways in PDGF-induced cell proliferation.

Results: Our results demonstrated that PDGF dose-dependently induced proliferation of primary cultured mouse renal fibroblasts; this effect was blocked by inhibition of PI3K/AKT signal pathway. PDGF also stimulated AKT-dependent mTOR activation and skp2 expression, elevation of skp2 in turn proteolysed p27 and caused cell proliferation. Activation of AMPK by metformin reduced PDGF-induced cell proliferation by suppression of AKT-driven mTOR activation. Our results indicate that activation of PI3K/AKT signaling and subsequent mTOR activation and skp2 expression mediated PDGF-induced renal fibroblasts proliferation.

Conclusion: This study suggests that activation of AMPK might be a novel strategy for the treatment of CKD partially by inhibition of renal interstitial fibrosis.

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Hybrid Renal Replacement Therapy in Treatment of Children with Acute Inflammatory Response Syndrome

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Objective: To investigate the efficacy of hybrid renal replacement therapy for patients with acute inflammatory response syndrome.

Methods: Retrospective analysis was performed on 30 children with acute renal failure and serious liver injury induced by mushroom poisoning, bee sting injury or severe pneumonia. The data of 30 cases were divided into group A (drug therapies and PE+CVVHDF, n = 17) and group B (only drug therapies, n = 13). The liver and kidney functions, the blood gas analysis, inflammatory factors and cure rates were compared between the two groups.

Results: All indexes and patients' condition in the two groups had no statistical differences before treatment. Compared with Group B, through combining CVVHDF+PE and drugs, AST (32.68 ± 19.52 vs. 306.4 ± 13.6 U/L), ALT (76.58 ± 36.44 vs. 418.7 ± 160.7 U/L) and Scr (92.73 ± 36.4 vs. 247.38 ± 126.64 $\mu\text{mol/L}$) could decline more markedly. CRP (5.3 ± 3.93 vs. 39.7 ± 28.63 mg/L), IL-6 (6.6 ± 3.52 vs. 67.35 ± 35.86 pg/L) and TNF- α

(98 ± 37 vs. 210 ± 47 pg/L) could be cleared more effectively in group A. Moreover, this hybrid renal replacement therapy was more conducive to regulate the acid-base balance in the body (pH 7.39 ± 0.05 vs. 7.33 ± 0.16 ; PCO₂ 35.7 ± 5.8 vs. 39.8 ± 7.2 mmHg; HCO₃⁻ 25.8 ± 1.63 vs. 18.8 ± 5.91 mmol/L). The cure rate of group A was apparently higher than that of group B (100% vs. 55.5%, $P < 0.001$).

Conclusion: On the basis of routine treatment, early application of hybrid renal replacement therapy for patients with acute inflammatory response syndrome caused by mushroom poisoning, bee sting injury or severe pneumonia could make various toxins in the blood circulation be removed and greatly restore the organs' function and improve cure rates.

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Macrophages Involved in Kidney Disease

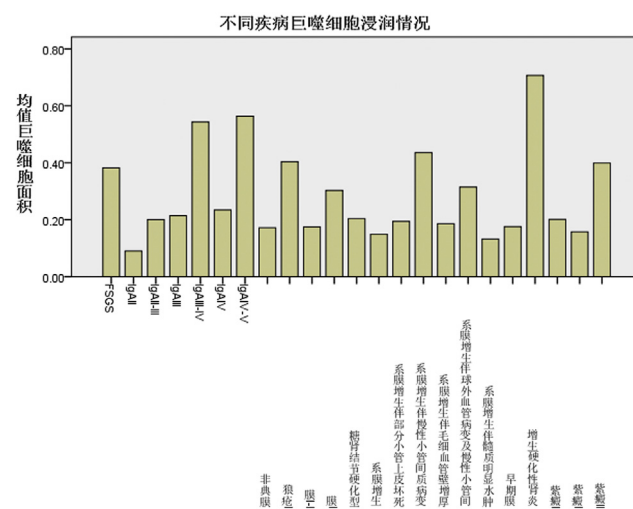
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Objective: This study is about the relationship between kidney disease and the type of macrophages infiltration, and to discover the therapy of chronic kidney disease.

Methods: We choose 47 cases of renal biopsy specimens, including 6 cases of mesangial proliferative glomerulonephritis, 7 cases of mesangial proliferative with chronic interstitial or vascular disease, 11 cases of membranous nephropathy, 11 cases of IgA nephropathy, five cases of diabetic nephropathy, 2 cases of FSGS, 3 cases of purpura nephritis, 1 case of lupus nephritis, 1 case of proliferative sclerosing glomerulonephritis. All the cases are stained with CD68 immunohistochemical method. Using ImageJ and SPSS 18.0 software, we get the relationships between different types of kidney disease and degree of macrophage infiltration.

Results: Macrophage infiltration is mainly in the tubulointerstitial area. Macrophage infiltration in various types of diseases are as follows: mesangial proliferative glomerulonephritis is 14.9%, mesangial proliferation with chronic interstitial or vascular disease is 26.92%, membranous nephropathy is 18.52%, IgA is 32.56%, diabetic nephropathy is 20.41%, FSGS is 38.20%, purpura nephritis is 25.27%, lupus nephritis is 40.4%, proliferative sclerosing glomerulonephritis is 70.69%.

Conclusion: By analyzing the morphological of different diseases macrophage infiltration, we can see that IgA nephropathy, lupus nephritis, mesangial proliferation with chronic tubulointerstitial disease, sclerosis nephritis, purpura nephritis have more macrophage infiltration.



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